IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: DIET DRUGS (PHENTERMINE/ FENFLURAMINE/DEXFENFLURAMINE) PRODUCTS LIABILITY LITIGATION	:	MDL DOCKET NO. 1203
THIS DOCUMENT RELATES TO:	:	
SHEILA BROWN, et al.	:	CIVIL ACTION NO. 99-20593
v.	:	
AMERICAN HOME PRODUCTS CORPORATION	:	2:16 MD 1203

MEMORANDUM IN SUPPORT OF SEPARATE PRETRIAL ORDER NO. 9478

Bartle, J. October 17, 2016

The Estate of Alice F. Wilson ("Estate"), a representative claimant under the Diet Drug Nationwide Class Action Settlement Agreement ("Settlement Agreement") with Wyeth,[1] seeks benefits from the AHP Settlement Trust ("Trust"). Based on the record developed in the show cause process, we must determine whether the Estate has demonstrated a reasonable medical basis to support its claim for Matrix Compensation Benefits ("Matrix Benefits").[2]

1. Prior to March 11, 2002, Wyeth was known as American Home Products Corporation. In 2009, Pfizer, Inc. acquired Wyeth.

2. Matrix Benefits are paid according to two benefit matrices (Matrix "A" and Matrix "B"), which generally classify Diet Drug Recipients for compensation purposes based upon the severity of their medical conditions, their ages when they are diagnosed,

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To seek Matrix Benefits, a representative claimant[3] must first submit a completed Green Form to the Trust. The Green Form consists of three parts. The representative claimant completes Part I of the Green Form. Part II is completed by an attesting physician, who must answer a series of questions concerning the Diet Drug Recipient's medical conditions that correlate to the Matrix criteria set forth in the Settlement Agreement. Finally, if the representative claimant is represented by an attorney, the attorney must complete Part III.

Under the Settlement Agreement, only eligible claimants or representative claimants are entitled to Matrix Benefits. Generally, a claimant or representative claimant is considered eligible for Matrix Benefits if the Diet Drug

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and the presence of other medical conditions that also may have caused or contributed to the Diet Drug Recipient's valvular heart disease ("VHD"). See Settlement Agreement §§ IV.B.2.b. & IV.B.2.d.(1)-(2). Matrix A-1 describes the compensation available to representative claimants where the Diet Drug Recipients were diagnosed with serious VHD, they took the drugs for 61 days or longer, and they did not have any of the alternative causes of VHD that made the B matrices applicable. In contrast, Matrix B-1 outlines the compensation available to representative claimants where the Diet Drug Recipients were registered as having only mild mitral regurgitation by the close of the Screening Period, they took the drugs for 60 days or less, or they were diagnosed with conditions that would make it difficult for them to prove that their VHD was caused solely by the use of these Diet Drugs.

3. Under the Settlement Agreement, representative claimants include estates, administrators or other legal representatives, heirs, or beneficiaries. See Settlement Agreement § II.B.

Recipient is diagnosed with mild or greater aortic and/or mitral regurgitation[4] by an echocardiogram performed between the commencement of Diet Drug use and the end of the Screening Period.[5] See id. §§ IV.B.1.a. & I.22.

In 2014, Charles T. Long[6] submitted a Green Form to the Trust signed by the attesting physician, Robert L. Rosenthal, M.D. Based on an echocardiogram dated May 3, 2011,[7] Dr. Rosenthal attested in Part II of the Green Form that Ms. Wilson had moderate mitral regurgitation, surgery to repair or replace the aortic and/or mitral valve(s) following the use of Pondimin® and/or Redux™, and ventricular fibrillation or sustained ventricular tachycardia which results in hemodynamic

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4. Under the Settlement Agreement, mild mitral regurgitation is defined as "(1) either the RJA/LAA ratio is more than five percent (5%) or the mitral regurgitant jet height is greater than 1 cm from the valve orifice, and (2) the RJA/LAA ratio is less than twenty percent (20%)." Settlement Agreement § I.38.

5. The Screening Period ended on January 3, 2003 for echocardiograms performed outside of the Trust's Screening Program and on July 3, 2003 for echocardiograms performed in the Trust's Screening Program. See id. § I.49.

6. Mr. Long did not identify his legal relationship to the Diet Drug Recipient, Alice F. Wilson ("Ms. Wilson"). In June, 2015, Jan S. Dillman, administrator of the Estate, submitted an amended Part I of the Green Form.

7. Because Ms. Wilson's May 3, 2011 echocardiogram was performed after the end of the Screening Period, the Estate relied on an echocardiogram dated April 3, 2002 to establish eligibility to receive Matrix Benefits.

compromise.[8] Based on such findings, the Estate would be entitled to Matrix B-1,[9] Level V[10] benefits in the amount of $116,993.

In the report of Ms. Wilson's April 3, 2002 echocardiogram, the reviewing cardiologist, Bradley M. Leonard, M.D., F.A.C.C., stated that Ms. Wilson had moderate mitral regurgitation. Dr. Leonard, however, did not specify a percentage as to the level of Ms. Wilson's mitral regurgitation. Under the definition set forth in the Settlement Agreement, moderate or greater mitral regurgitation is present where the

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8. Dr. Rosenthal also attested that Ms. Wilson suffered from aortic stenosis, pulmonary hypertension secondary to moderate or greater mitral regurgitation, an abnormal left atrial dimension, a reduced ejection fraction in the range of 50% to 60%, and New York Heart Association Functional Class I symptoms. These conditions are not at issue in this claim.

9. The Estate did not contest the Trust's determination that Ms. Wilson had mitral annular calcification. Under the Settlement Agreement, the presence of mitral annular calcification requires the payment of reduced Matrix Benefits for a claim based on damage to the mitral valve. See id. § IV.B.2.d.(2)(c)ii)d).

10. Under the Settlement Agreement, a representative claimant is entitled to Level V benefits if the Diet Drug Recipient qualifies for Level III Matrix Benefits and suffered from ventricular fibrillation or sustained ventricular tachycardia which results in hemodynamic compromise. See Settlement Agreement § IV.B.2.c.(5)(d). A representative claimant is entitled to Level III benefits if the Diet Drug Recipient suffered from "left sided valvular heart disease requiring . . . [s]urgery to repair or replace the aortic and/or mitral valve(s) following the use of Pondimin® and/or Redux." Id. § IV.B.2.c.(3)(a).

Regurgitant Jet Area ("RJA"), in any apical view, is equal to or greater than 20% of the Left Atrial Area ("LAA"). See Settlement Agreement § I.22.

In or around July, 2015, the Trust forwarded the claim for review by M. Michele Penkala, M.D., one of its auditing cardiologists. In audit, Dr. Penkala determined that there was no reasonable medical basis for finding that Ms. Wilson had at least mild mitral regurgitation between the commencement of Diet Drug use and the end of the Screening Period. Specifically, Dr. Penkala explained:

> Based on my review of both copies of the [transthoracic echocardiogram] dated 4/3/02 I do not find ANY significant [mitral regurgitation]. There is at most a tiny jet of typical "backflow" as the "traced [mitral regurgitant] jet" occurring in early systole on the QRS during the "red-blue" phase of the cardiac cycle."

Based on the auditing cardiologist's findings, the Trust issued a post-audit determination denying the Estate's claim. Pursuant to the Rules for the Audit of Matrix Compensation Claims ("Audit Rules"), the Estate contested this adverse determination.[11] In contest, the Estate argued that

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11. Claims placed into audit on or before December 1, 2002 are governed by the Policies and Procedures for Audit and Disposition of Matrix Compensation Claims in Audit, as approved in Pretrial Order ("PTO") No. 2457 (May 31, 2002). Claims placed into audit after December 1, 2002 are governed by the Audit Rules, as approved in PTO No. 2807 (Mar. 26, 2003). There

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there was a reasonable medical basis for finding that Ms. Wilson had at least mild mitral regurgitation between the commencement of Diet Drug use and the end of the Screening Period. According to the Estate, the reasonable medical basis standard is a "relatively low threshold." In addition, the Estate contended that the auditing cardiologist either did not review multiple loops and frames or she "simply decided to ignore the evidence that was favorable to the Claimant." Finally, the Estate submitted a declaration of Paul W. Dlabal, M.D., F.A.C.P., F.A.C.C., F.A.H.A., wherein he stated:

> 3. At time 5:35, the mitral valve regurgitant jet area (RJA) was traced and measured by the technician at 1.15 cm^2 (RJA/LAA = 1.15 cm^2/9.3 cm^2 = 12.4%). By visual inspection, I found that the RJA measured 0.85 cm^2 (RJA/LAA = 0.85 cm^2/9.3 cm^2 = 9.1%). This regurgitant jet was colored blue and yellow.
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> 4. I found another regurgitant jet at time 5:54. By visual inspection, I found that the RJA measured 1.0 cm^2 (RJA/LAA = 1.0 cm^2/9.3 cm^2 = 10.8%). The regurgitant jet was colored blue.
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> 5. At time 6:03, I found an orangish yellow regurgitant jet which was timely and properly traced and measured by the technician at 0.77 cm^2 (RJA/LAA = 0.77 cm^2/9.3 cm^2 = 8.3%). This jet was the easiest to see, and it was accurately traced by the technician.

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is no dispute that the Audit Rules contained in PTO No. 2807 apply to the Estate's claim.

6. I found that the RJA/LAA ratio ranged from 8.3% to 10.8%, with an average ratio of 9.4%.

7. These jets were very consistent in the 4-chamber (apical) view, and they involved only the lateral portion of the mitral valve. Further, these jets were true regurgitant jets which were representative of other jets in the mild range.

8. These jets were pathological regurgitant jets, and they were not "backflow." In fact, there were no incidences of "backflow" in the 4-chamber view.

9. Each of these jets originated from the mitral valve and spread into the left atrium during a portion of systole. They occurred following the QRS complex. The left ventricle was fully contracted, and the mitral valve was closed. These jets did not occur as a result of the closing of the mitral valve.

10. When considering the velocities and durations of these jets, none of them could be classified as "backflow." Further, an average RJA/LAA ratio of 9.4% is not consistent with "backflow."

11. An alleged "red-blue" phase of a cardiac cycle is very confusing. It is not a term used by a clinician. With Color Flow Doppler, blood flow that is moving away from the transducer will appear as blue, while blood flow moving toward the transducer will appear as red. Therefore, red and blue colors will always appear during the cardiac cycle.

12. As in this case, true mitral valve regurgitant jets occurring during systole may be blue, green, mosaic, or multi-colored with blue, green, and yellow stripes. The color of the jets in this case did not suggest "backflow."

> 13. My findings established a reasonable medical basis in support of pathological mitral valve regurgitation which would be classified as mild in accord with the Singh criteria. Contrary to the claims made by the Trust's doctor, there was no evidence of "backflow" found in the 4-chamber (apical) view.

Although not required to do so, the Trust forwarded the claim for a second review by the auditing cardiologist. Dr. Penkala submitted a declaration in which she again concluded that Ms. Wilson did not have at least mild mitral regurgitation between the commencement of Diet Drug use and the end of the Screening Period. Specifically, Dr. Penkala stated, in pertinent part:

> 11. I re-reviewed the VHS and CD copies of Ms. Wilson's April 3, 2002 Eligibility Echocardiogram in great detail. I specifically evaluated the study at the times noted in the letters from Dr. Dlabal and Mr. Hudson. All of the "jets" mentioned by Dr. Dlabal are very brief duration, low velocity color flow occurring at the beginning of or on the QRS. The frames at 5:35 and 5:54 are both very small regions of flow within the "red-blue" portion of the cardiac cycle. At the other time noted in the letter (6:03) there is in fact NO color and thus no evidence of flow whatsoever. At 6:01 (a time NOT mentioned in the letter) there is once again a very small traced region of flow with the same qualities noted above—not true [mitral regurgitation].
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> 12. There is continuous wave Doppler interrogation of the mitral valve at approximately 6:59 and again at 7:05. At these times there is clear mitral valve inflow seen in diastole from the left atrium

> across the mitral valve into the left ventricle. There is no evidence of mitral regurgitation in this same tracing.

The Trust then issued a final post-audit determination again determining that the Estate was not entitled to Matrix Benefits. The Estate disputed this final determination and requested that the claim proceed to the show cause process established in the Settlement Agreement. See Settlement Agreement § VI.E.7.; PTO No. 2807, Audit Rule 18(c). The Trust then applied to the court for issuance of an Order to show cause why the Estate's claim should be paid. On March 7, 2016, we issued an Order to show cause and referred the matter to the Special Master for further proceedings. See PTO No. 9460 (Mar. 7, 2016).

Once the matter was referred to the Special Master, the Trust submitted its statement of the case and supporting documentation. The Estate then served a response upon the Special Master. The Trust submitted a reply on May 5, 2016, and the Estate submitted a sur-reply on May 24, 2016. Under the Audit Rules, it is within the Special Master's discretion to appoint a Technical Advisor[12] to review claims after the Trust

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12. A "[Technical] [A]dvisor's role is to act as a sounding board for the judge -- helping the jurist to educate himself in the jargon and theory disclosed by the testimony and to think through the critical technical problems." Reilly v. United States, 863 F.2d 149, 158 (1st Cir. 1988). In a case such as (continued . . .)

and the Estate have had the opportunity to develop the show cause record. See Audit Rule 30. The Special Master assigned a Technical Advisor, Gary J. Vigilante, M.D., F.A.C.C., to review the documents submitted by the Trust and the Estate and to prepare a report for the court. The Show Cause Record and Technical Advisor Report are now before the court for final determination. See id. Rule 35.

The issue presented for resolution of this claim is whether the Estate has met its burden of proving that there was a reasonable medical basis for finding that Ms. Wilson had at least mild mitral regurgitation between the commencement of Diet Drug use and the end of the Screening Period. See id. Rule 24. Ultimately, if we determine that there is no reasonable medical basis for the finding that is at issue, we must affirm the Trust's final determination and may grant such other relief as deemed appropriate. See id. Rule 38(a). If, on the other hand, we determine that there is a reasonable medical basis for the finding, we must enter an Order directing the Trust to pay the claim in accordance with the Settlement Agreement. See id. Rule 38(b).

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this where conflicting expert opinions exist, it is within the discretion of the court to appoint a Technical Advisor to aid it in resolving technical issues. Id.

In support of its claim, the Estate repeats the arguments raised in contest, namely, that there is a reasonable medical basis for the representation that Ms. Wilson had at least mild mitral regurgitation between the commencement of Diet Drug use and the end of the Screening Period. In addition, the Estate contends that the Trust blindly accepted the findings of the auditing cardiologist without considering the reasonable findings of the Estate's doctors. The Estate also submitted a supplemental declaration from Dr. Dlabal in which he stated:

> 3. At times 5:53 and 5:54, I found true regurgitant jets which are in the mild range, as described in my previous declaration dated 11/6/15. As I also stated, these regurgitant jets follow the QRS complex, and last through a portion of systole.
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> 4. The durations of these jets and the colors of these jets do not even suggest a lack of mild mitral regurgitation (MR). Instead, these jets represent mild [mitral regurgitation] in accord with the Singh criteria.
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> 5. Moreover, there is a more dramatic burst of [mitral regurgitation] at 5:35, as reported in ¶ 3 of my prior declaration. The jet is bright, blue-yellow, traced and measured by the technician, and clearly indicates at least mild [mitral regurgitation]. If this is not enough, there is also a spontaneous episode of [mitral regurgitation] in the [parasternal long-axis] view at 1:24-25. These jets are central in the atrium and yellow-orange, thus indicating aliasing or high velocity jets.

6. Again, an alleged "red-blue" phase of the cardiac cycle makes no sense. There is no such thing. As I explained earlier, images are either red or blue, unless multi-colored aliasing is involved.

7. At time 6:03, I can grant that there is color dropout on the CD, presumably after many copies, and even deterioration of the original videotape prior to copying. Nevertheless, the technician was sufficiently impressed that he or she stopped to encircle this very image, and I have reported it as such in ¶ 5 of my declaration. The color is more accurately described as blue with red-yellow aliasing.

8. With regard to time 6:01, I will refer to the preceding paragraph of this supplement. First, it appears that this is the same beat as reported in the preceding paragraph concerning time 6:03. Second, I disagree that the regurgitant flow occurs only on the QRS. Third, even if one excludes this beat, the exclusion does not invalidate the numerous other findings above. I did not cite anything about an image at 6:01 in my prior declaration, nor do I see anything separate from the beat at 6:03, so I have no idea as to Dr. Penkala's meaning regarding this beat. If indeed, she meant to comment on the beat at 6:03, I have addressed this above.

9. At times 6:59 and 7:05, I grant that the continuous wave (CW) Doppler does not show a distinct image of [mitral regurgitation], which it may not when [mitral regurgitation] is mild. [Continuous wave] is a "compressed" format for Doppler, designed to image very large jets on one screen without artefactual aliasing. More properly, the pulsed wave (PW) images are designed for smaller flow jets, and in this study, there are suggestions of confirmatory [mitral regurgitation] by [pulsed wave] Doppler at times 6:47-49 and again at 7:16. In the case of [pulsed wave] Doppler on the

> study, there is aliasing of the signal, which is suggestive of [mitral regurgitation].

In response, the Trust argues that Dr. Penkala properly applied the reasonable medical basis standard, which "requires an Auditing Cardiologist to use both 'normal clinical judgment' and 'accepted medical standards,'" to determine that Ms. Wilson did not have at least mild mitral regurgitation between the commencement of Diet Drug use and the end of the Screening Period.

The Technical Advisor, Dr. Vigilante, reviewed Ms. Wilson's echocardiograms. He concluded that there was no reasonable medical basis for finding that she at least mild mitral regurgitation between the commencement of Diet Drug use and the end of the Screening Period. In particular, Dr. Vigilante determined that there was no more than trace mitral regurgitation on Ms. Wilson's April 3, 2002 echocardiogram.[13] He stated in relevant part:

> I reviewed the tape and DVD of the Claimant's Eligibility echocardiogram. Both copies demonstrated the same study. This study was dated April 3, 2002. . . . This was a somewhat below quality and grainy study but was diagnostic. There was a lack

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13. As noted in the Report of Auditing Cardiologist Opinions Concerning Green Form Questions at Issue, trace, trivial, or physiologic regurgitation is defined as a "[n]on-sustained jet immediately (within 1 cm) behind the annular plane or <+ 5% RJA/LAA."

of color flow interrogation of the mitral valve in the apical two chamber view. The Nyquist limit was set low at 51 cm per second at a depth of 19 cm in the parasternal and apical views. However, the color flow evaluation was diagnostic in the study. . . . No mitral regurgitation was seen in real-time evaluation on color flow mapping in the parasternal long-axis view. In the apical four chamber view, there was just several pixels of mitral regurgitation seen on color flow mapping. This minimal regurgitation was all within 1 cm of the mitral valve annulus. There was no regurgitant jet that went beyond 1 cm of the mitral annulus. The time frames documented by Dr. Dlabal in his Declarations were evaluated. At most, only trace mitral regurgitation was noted at these time frames. At time frame 5:35, the sonographer had erroneously traced an RJA of 1.15 cm2. This contained a great amount of non-mitral regurgitant low velocity flow. At 5:54 on the study, there is only minimal mitral regurgitation within 1 cm of the valve annulus. At 6:03 on the tape, the sonographer erroneously traced a supposed RJA of 0.77 cm2. This also contained a great deal of low velocity, non-mitral regurgitant flow. There was not a single cardiac cycle that demonstrated mitral regurgitation beyond 1 cm of the mitral valve. This study was diagnostic of trace mitral regurgitation.

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[T]here is no reasonable medical basis to conclude that decedent's April 3, 2002 echocardiogram revealed the presence of at least mild mitral regurgitation. As documented above, there was no more than trace mitral regurgitation noted on the study. The mitral regurgitant jet was never more than 1 cm beyond the mitral valve annulus. An echocardiographer could not reasonably conclude that at least mild

> mitral regurgitation was present on this echocardiogram even taking into consideration of the issue of inter-reader variability.

In response to the Technical Advisor Report, the Estate argues that, unlike Dr. Dlabal, Dr. Vigilante did not provide measurements that supported his conclusions. In addition, claimant contends that Dr. Vigilante "refuted" the auditing cardiologist's finding that Ms. Wilson's echocardiographer included backflow in her measurements.

After reviewing the entire Show Cause Record, we find that the Estate has failed to establish a reasonable medical basis for the claim. As an initial matter, we disagree with the Estate's characterization of the reasonable medical basis standard. We are required to apply the standards delineated in the Settlement Agreement and the Audit Rules. The context of these two documents leads us to interpret the reasonable medical basis standard as more stringent than the Estate contends and one that must be applied on a case-by-case basis. Here, Dr. Penkala determined in audit that there was no reasonable medical basis for concluding that the April 3, 2002 echocardiogram demonstrated at least mild mitral regurgitation. Contrary to the Estate's assertion, the opinion offered by the Estate's expert, Dr. Dlabal, does not establish a reasonable medical basis for the Estate's claim.

As we previously explained, conduct "beyond the bounds of medical reason" can include: (1) failing to review multiple loops and still frames; (2) failing to have a Board-Certified Cardiologist properly supervise and interpret the echocardiogram; (3) failing to examine the regurgitant jet throughout a portion of systole; (4) over-manipulating echocardiogram settings; (5) setting a low Nyquist limit; (6) characterizing "artifacts," "phantom jets," "backflow" and other low velocity flow as mitral regurgitation; (7) failing to take a claimant's medical history; and (8) overtracing the amount of a claimant's regurgitation. See Mem. in Supp. of Separate PTO No. 2640 at 9-13, 15, 21-22, 26 (Nov. 14, 2002).

The auditing cardiologist and the Technical Advisor each reviewed the echocardiogram and concluded that it demonstrated at most trace mitral regurgitation. Specifically, Dr. Penkala reviewed the time frames that Dr. Dlabal referenced in his declaration and concluded that they were "very brief" and that they were "low velocity color flow occurring at the beginning of or on the QRS." She also observed that several of the tracings by the sonographer did not include any evidence of mitral regurgitation at all.[14] Similarly, Dr. Vigilante reviewed

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14. For this reason as well, we reject the Estate's contention that the auditing cardiologist did not review multiple loops and (continued . . .)

Ms. Wilson's April 3, 2002 echocardiogram and the specific time frames identified by Dr. Dlabal. Dr. Vigilante concluded that the sonographer had "erroneously traced" the RJA to include "a great amount of non-mitral regurgitant low velocity flow."[15] Such an unacceptable practice cannot provide a reasonable medical basis for the resulting diagnosis that Ms. Wilson suffered from at least mild mitral regurgitation.

Finally, we disagree with claimant's argument that the use of visual estimation was improper. Although the Settlement Agreement specifies the percentage of regurgitation needed to qualify as having moderate mitral regurgitation, it does not require that actual measurements must be made on the echocardiogram. As we have explained, "'[e]yeballing' the regurgitant jet to assess severity is well accepted in the world of cardiology." See Mem. in Supp. of PTO No. 2640 at 15. Claimant essentially requests that we write into the Settlement Agreement a requirement that actual measurements of mitral regurgitation be made to determine whether a claimant qualifies

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frames and that she "simply decided to ignore the evidence that was favorable to the Claimant."

15. Thus, we also reject claimant's argument that Dr. Vigilante "refuted" the auditing cardiologist's findings. In any event, Dr. Vigilante independently determined that Ms. Wilson's April 3, 2002 echocardiogram did not demonstrate at least mild mitral regurgitation as defined by the Settlement Agreement.

for Matrix Benefits. There is no basis for such a revision, and claimant's argument is contrary to the "eyeballing" standards that we previously evaluated and accepted in PTO No. 2640. In any event, Dr. Vigilante specifically found that Ms. Wilson's "minimal regurgitation was all within 1 cm of the mitral valve annulus," which qualifies as trace mitral regurgitation under the Settlement Agreement.

For the foregoing reasons, we conclude that the Estate has not met its burden of proving that there is a reasonable medical basis for finding that Ms. Wilson had at least mild mitral regurgitation between the commencement of Diet Drug use and the end of the Screening Period. Therefore, we will affirm the Trust's denial of the Estate's claim for Matrix Benefits.